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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of

Woodward et al

Serial No: 08/876,937

Filed: June 16, 1997

For: NON-ACIDIC CYCLOPENTANE HEPTANOIC ACID, 2-CYCLOALKYL OR ARYLALKYL DERIVATIVES AS THERAPEUTIC AGENTS

Group Art Unit: 1621

Examiner: P. O'Sullivan

Box Appeal Brief
Honorable Commissioner of Patents and Trademarks
Washington, D.C. 20231

BRIEF ON APPEAL

Dear Sir:

This appeal is taken from the final rejection of all of the claims in an Examiner's action mailed February 13, 2001. Oral hearing is waived.

(1) REAL PARTY IN INTEREST

This patent application is assigned to Vision Pharmaceuticals L.P., having its principal place of business at 2525 Dupont Drive, Irvine, CA 92612.

(2) RELATED APPEALS AND INTERFERENCES

None.

(3) STATUS OF CLAIMS

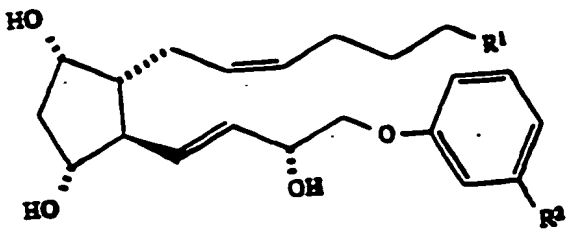
Claims	Status
26 through 45	Rejected under 35 USC § 102(e) as being anticipated by Bishop '383.
26-45	Rejected under 35 USC § 103(a) as being unpatentable over Bishop '383.
26, 28-34, 36-45 and 48	Rejected under 35 USC § 112, first paragraph as failing to include a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same.

(4) STATUS OF AMENDMENTS

No amendment or other responses were filed after the Final Rejection.

(5) SUMMARY OF THE INVENTION

The present invention provides a method of treating glaucoma and ocular hypertension which comprises topically administering to the affected eye a therapeutically effective amount of a compound of formula:



wherein R^1 =hydrogen, a cationic salt moiety, a pharmaceutically acceptable amine moiety or C_1-C_{12} alkyl cycloalkyl or aryl; and R^2 = Cl_1 or CF_3. (See claim 26.) Topical ophthalmic compositions useful in the method of the invention are also provided. (See claim 34.)

Claims 46 and 47 to the use of cloprostenol and fluprostenol, respectively, in treating glaucoma and ocular hypertension have been allowed but are subject to an interference.

(6) ISSUES

Enablement

Whether Applicants have provided a written description of the invention as defined in claims 26, 28-34, 36-45 and 48, in such a way as to reasonably convey to one skilled in the relevant art containing a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same?

Anticipation

Whether claims 26-45 lack novelty over United States Patent Number 5,510,383 to Bishop et al (Bishop '383)?

Obviousness

Whether claims 26-45 are obvious over Bishop '383?

(7) GROUPING OF CLAIMS

Group I, Enablement includes claims 26, 28 through 34, 36 through 45 and 48.

As discussed below, it is believed that claims 42 through 45 are not subject to rejection under 35 USC § 112, first paragraph, even if claims 26, 28 through 34, 36 through 41 and 48 are properly rejected.

Group II, Anticipation includes claims 26 through 45.

Group III, Obviousness includes claims 26 through 45

(8) ARGUMENT

ENABLEMENT

(i.) (B) The Rejection of the Claims of Group I Under 35 USC § 112, first Paragraph.

The Examiner has rejected claims 26, 28-34 and 36-45 under 35 USC § 112, first paragraph, because the specification, while being enabling for R^1 as H, lower alkyl or a cation, does not reasonably provide enablement for applicants' added groups. (By this the Examiner is excluding "a pharmaceutically acceptable amine moiety or…cycloalkyl or aryl" from the definition of R^1.) The Examiner argues that "specification does not enable any person skilled in the art to which it pertains, or with which it is most clearly connected, to make and/or use the invention commensurate in scope with these claims."

The Examiner has cited, as prior art, Bishop et al U.S. Patent 5,510,383 (hereinafter Bishop et al or Bishop '383), discussed below, in his rejection under USC § 102(e) and 103(a). The claims of the present application were copied from Bishop et al. In Bishop et al the various ester groups

that the Examiner insists are not enabled by applicants' specification are discussed, at from Column 3, line 65 through Column 4, line 9. In Bishop et al, it is made clear that all such ester groups, including cycloalkyl or aryl are made by conventional procedures. For example, at lines 7 and 8 of Column 4 of Bishop et al it is stated that "(s)ince such esterification reactions are well known, they are not further described here." As to the excluded amine moiety, it is believed that such amine is disclosed in Bishop et al as a salt. (See column 3, line 55.) And Bishop et al states that salts can be conventionally formed from the acid form. (See column 3, lines 64 and 65 of Bishop et al wherein, as to the formation of the alkali or alkali metal salts, salt formation is described as conventional.) Thus, clearly Bishop et al, which the Examiner cites as prior art to the applicants' claims 26, 28-34 and 36-45, supports applicants' argument that <u>making</u> compounds with all of the R^1 groups claimed by applicant is within the ordinary skill of the art.

The Examiner responds by arguing that although "applicants argue that since Bishop et al '383 teach conventional methods may be used to make some compounds that it would have been obvious how to make applicants' added compounds, 35 USC § 112, first paragraph, concerns not only the making of an invention but using it well. Applicants do not show how to use the newly added groups in their original specification."

However, it is clear that applicant has taught that all of the compounds, wherein R^1 is other than H, lower alkyl or a cation, may be <u>used</u> to treat glaucoma and ocular hypertension. In Examples 6 and 7 a method for evaluating applicants' compounds for such use is disclosed. One of

ordinary skill in the art could use the methodology of Examples 6 and 7 to evaluate any and all of the compounds, having R^1 groups that Examiner argues are not enabled, for treating glaucoma and ocular hypertension.

Thus, it is believed that in accordance with 35 USC § 112, first paragraph, applicants have shown how to make and use the claimed invention commensurate in scope with claims 26, 28-34 and 36-45.

Alternatively, it is not understood how the Examiner can argue that the present claims are not enabled if the prior art asserted by the Examiner, i.e. Bishop et al, with the same disclosure, issued claims that are enabled. Note that Bishop et al in his working Examples shows only the activity of the 1-isopropyl esters of fluprostenol and cloprostenol. The remainder of Bishop et al's disclosure is equivalent of the applicants' disclosure, i.e. Bishop et al did not specifically demonstrate that a "pharmaceutically acceptable amine moeity or a cyclo alkyl or aryl" radical would function as an isopropyl ester in fluprostenol or cloprostenol for treating glaucoma or ocular hypertension.

(It is noted that claims 27 and 35, wherein R^1 is H, CH_3, $CH(CH_3)_2$ or $C(CH_3)_3$ are not rejected under 35 USC § 112. The significance of this failure to reject claims 27 and 35 under 35 USC § 112 is discussed below.)

Not withstanding the above argument, it is not understood why the Examiner has rejected claims 42 through 45 under 35 USC § 112, first paragraph, since when R^1 is lower alkyl in claim 1 of Bishop et al and present claim 26, as the Examiner agrees is supported by the present specification, the 1 position of the compound of the formula of said claim 1 of Bishop et al and said claim 26 of the present application, is an ester moiety, as required by

applicants' claims 42 through 45. The Examiner states regarding claims 42-45, "an acceptable ester moiety" would include groups other than alkyl which are not enabled by applicants' specification. Alkyl esters are only one type of ester." However, since claims 27 and 35 which are limited to "acceptable ester moieties", i.e. the alkyl esters, are not rejected for lack of enablement under 35 USC § 112, first paragraph, it is not understood why claims 42-45 are not also enabled by applicant's specification. Therefore, the Board is specifically requested to overrule the Examiner's rejection of claims 42 through 45 under 35 USC § 112, first paragraph.

ANTICIPATION

(iii) The Rejection of Claims 26-45 under 35 USC § 102(e).

The Examiner has rejected claims 26-45 under 35 USC § 102(e) as being anticipated by Bishop et al. As stated above, claims 26-45 of this application have been copied from U.S. Patent 5,510,383, i.e. Bishop et al, to provoke an interference. (Claims 26-45 were first copied in U.S. Patent Application Serial No. 08/605,567, the parent of the present application, which has a filing date of February 22, 1996, i.e. earlier than the April 23, 1996, issue date of Bishop et al.)

The Examiner rejected Claims 26-45 under 35 USC § 102(e) as being anticipated by Bishop et al which discloses and claims the use of cloprostenol, fluprostenol, etc. to treat glaucoma and ocular hypertension. (See the Title of Bishop et al.) The Examiner has previously argued that (t)hese claims are not patentable to the applicant because they are rejected under 35 USC § 112, first

paragraph and under 35 USC § 102(e) above, and "an interference cannot be initiated since a prerequisite for interference under 37 CFR § 1.606 is that claims be patentable to the applicant subject to a judgement in the interference." (Note, the Examiner is stating that no interference can be declared because claims 26-45 are not patentable under 35 USC § 112, first paragraph. However, as discussed above, the Examiner has not rejected claims 27 and 35 under 35 USC § 112, first paragraph. Therefore as to these claims, at least, the 35 USC § 102(e) rejection is clearly incorrect. Moreover, even if the Examiner is right as to claims 26, 28 through 34 and 36 through 41, applicants believe, as argued above, that the Examiner is incorrect in his rejection of claims 42-45 under 35 USC § 112, first paragraph.)

Moreover, the applicants wish to point out that these claims 26 through 45 are also supported in U.S. Patent Application 07/948,056, the Grandparent of the present Application having a filing date of September 21, 1992 (which predates the filing date of Bishop '383) as follows:

It is clear that the applicants disclose in the Grandparent Application, the compound 16-m-chlorophenoxy $PGF_{2\alpha}$, i.e. cloprostenol which is the corresponding acid of the isopropyl ester designated as A in Table 1 of Bishop '383. (The acid, i.e. cloprostenol, is included in claim 1 of Bishop '383, i.e. where R^1 is hydrogen and R^2 is chlorine.) This compound is also shown at Table V of the Grandparent Application to be an effective IOP lowering agent both as an acid and as the 1-hydroxyl and 1-amido derivatives thereof. Note the methyl ester and the amido derivatives of 16-m-chloro phenoxy $PFG_{2\alpha}$, i.e. cloprostenol, are prepared in Examples 8 and 9 of the

Grandparent Application while the 1-hydroxy derivative is prepared in Example 15 of the Grandparent Application.

The applicants also submitted a Declaration Under Rule 1.131 in the '567 Application which demonstrates that, prior to the filing date of Bishop '383, the applicants had reduced to practice the present invention as related to fluprostenol in the United States." (A copy of the Declaration under 37 CFR § 1.131 was filed in the present application for the Examiner's reference.) Fluprostenol is the corresponding acid of the isopropyl ester designated as B in Table 1 of Bishop et al and is also included in claim 1 of Bishop '383, when R^1 is hydrogen and R^2 is CF_3.

Thus, as to the compounds upon which the invention of Bishop '383 is based, i.e. cloprostenol and floprostenol, applicants have either an earlier filing date or declaration showing a reduction to practice prior to the filing date of Bishop '383. The further disclosure of Bishop '383, that the acids cloprostenol and fluprostenol may be esterified or converted to a pharmaceutically acceptable salt for the purpose of treating glaucoma or ocular hypertension may be shown to be obvious in view of applicants showing of the same activity for said acids.

Furthermore, applicants believe that under 35 USC § 102(g) Bishop's claims may not be patentable since applicants believe that they may be able to show that the invention of Bishop "was made in this country by another", i.e. Woodward et al, prior to the date of invention by Bishop. The Declaration under 35 USC § 131 was filed to show Woodward et al made the invention before Bishop et al's filing date. The Board is referred to Bates v. Coe 98 U.S. 31, 34 (1878) wherein it is stated that "the presumption in respect to the invention described in the patent in suit, if it is accompanied by the application for the same, is that it was made at the time the application was filed; and the

complainant or plaintiff may, if he can, introduce proof to show that it was made at a much earlier date."

Thus, for two reasons, the Examiner is incorrect in his rejection under 35 USC § 102(e):

First, applicants are entitled to prove in an interference that they are the prior inventors and entitled to a patent on the invention defined in claims 26 through 45.

Second, the patentees, i.e. Bishop et al, may not be entitled to the patent under 35 USC § 102(g) since they were not the first to make the invention.

In summary, if the Examiner can take the position that in order to provoke an interference an applicant must show support for the claims according to 35 USC § 112, first paragraph, in an application that predates the filing date of a patent, then under U.S. Patent Law the first to file, not the first to invent, will obtain the patent. This is clearly not the law.

OBVIOUSNESS

(iv) The Rejection of the Claims 26-45 under 35 USC § 103. For reasons given above regarding the Examiner's rejection of claims 26-45 as anticipated by Bishop et al, it is believed that the applicants disclosed the subject matter of such claims prior to Bishop et al. Therefore, it is believed that the claims are not properly rejected over Bishop et al under 35 USC § 103.

In view of the above, the Board is asked to reverse the Examiner's holding of all of the pending claims as unpatentable and direct the Examiner to pass the claims to issue.

Respectfully submitted,

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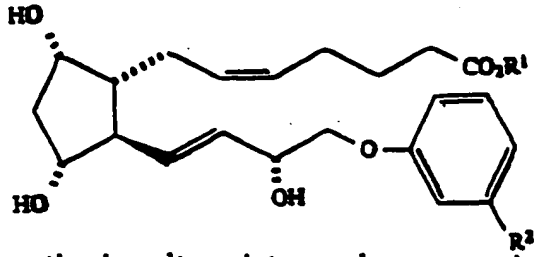
CERTIFICATE OF MAILING

I HEREBY CERTIFY THAT THIS CORRESPONDENCE IS BEING DEPOSITED WITH THE UNITED STATES POSTAL SERVICE AS FIRST-CLASS MAIL IN AN ENVELOPE ADDRESSED TO: BOX APPEAL BRIEF COMMISSIONER OF PATENTS AND TRADEMARKS, WASHINGTON, D.C. 20231 ON 12/13/01 Printed name of person making deposit: Bonnie Ferguson Signature of person making deposit: Bonnie Ferguson Date Signed: 12/13/01

(7) APPENDIX

CLAIMS:

26. A method of treating glaucoma and ocular hypertension which comprises topically administering to the affected eye a therapeutically effective amount of a compound of formula:



wherein R^1 =hydrogen, a cationic salt moiety, a pharmaceutically acceptable amine moiety or C_1-C_{12} alkyl cycloalkyl or aryl; and R^2 = Cl or CF_3.

27. The method of claim 26, wherein R^1 is selected from the group consisting of H, CH_3, $CH(CH_3)_2$ and $C(CH_3)_3$.

28. The method of claim 26, wherein R^1 is selected from the group consisting of Na^+ and $CH_3N^+(CH_2OH)_3$.

29. The method of claim 26, wherein R^2 is Cl.

30. The method of claim 27, wherein R^2 is CF_3.

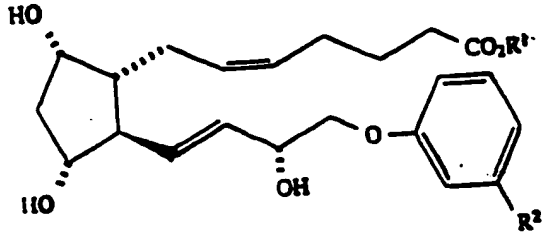
31. The method of claim 26, wherein between about 0.001 and about 1000 µg/eye of a compound of formula (I) is administered.

32. The method of claim 31, wherein between about 0.01 and about 100 µg/eye of a compound of formula (I) is administered.

33. The method of claim 31, wherein between about 0.05 and about 10 µg/eye of a compound of formula (I) is administered.

(7) APPENDIX (Cont.)

34. A topical ophthalmic composition for the treatment of glaucoma and ocular hypertension in primates, comprising a therapeutically effective amount of a compound of formula:



wherein: R^1 = hydrogen, a cationic salt moiety, a pharmaceutically acceptable amine moiety or C_1-C_{12} alkyl, cycloalkyl or aryl; and R^2 = Cl or CF_3.

35. The composition of claim 34, wherein R^1 is selected from the group consisting of H, CH_3, $CH(CH_3)_2$ and $C(CH_3)_3$.

36. The composition of claim 34, wherein R^1 is selected from the group consisting of Na^+ and $CH_3N^+(CH_2OH)_3$.

37. The composition of claim 34, wherein R^2 is Cl.

38. The composition of claim 34, wherein R^2 is CF_3.

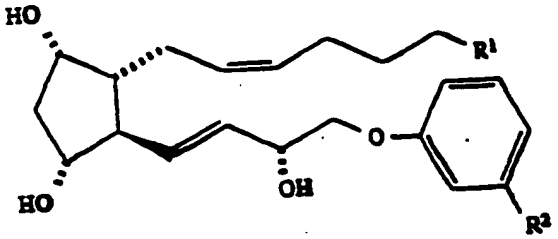
39. The composition of claim 34, wherein between about 0.001 and about 100 µg/eye of a compound of formula (I) is administered.

40. The composition of claim 39, wherein between about 0.01 and about µg/eye of a compound of formula (I) is administered.

(7) APPENDIX (Cont.)

41. The composition of claim 40, wherein between about 0.05 and about 10 μg/eye of a compound of formula (I) is administered.

42. A method of treating glaucoma and ocular hypertension, which comprises topically administering to the affected eye a therapeutically effective amount of a compound of formula:



wherein: R^1 = a pharmaceutically acceptable ester moiety; and R^2 = Cl or CF_3.

43. The method of claim 42, wherein R^2 is Cl.

44. The method of claim 42, wherein R^2 is CF_3.

45. The method of claim 42, wherein between about 0.001 and about 1000 μg/eye of a compound of formula (I) is administered.

(7) APPENDIX (Cont.)

46. A method of treating glaucoma and ocular hypertension which comprises topically administering to the affected eye a therapeutically effective amount of cyclopentane heptenoic acid, 5-cis-2-(3-α-hydroxy-4-m-chlorophenoxy-1-trans-butenyl)-3,5-dihydroxy 1_α, 2_β, 3_α, 5_α].

47 A method of treating glaucoma and ocular hypertension which comprises topically administering to the affected eye a therapeutically effective amount of fluprostenol.

48 A topical ophthalmic composition for the treatment of glaucoma and ocular hypertension in primates, comprising a therapeutically effective amount of fluprostenol.